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SYNTHESIS, SPECTRAL AND BIOLOGICAL PROPERTIES OF 4-AMINOANTIPYRINE-BASED SCHIFF BASE TRANSITION METAL COMPLEXES.

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ABSTRACT
4-aminoantipyrine moiety containing Schiff bases mono nuclear complexes has been synthesized by reaction of transition metals (CO, Zn, and Cd). Their characterisations involved FTIR, UV-Vis, ^{1}H-NMR and elemental analysis. The transition metal complexes shows moderate to excellent antifungal activity and anti-bacterial activity. The synthesis of new potential metal based drug.

KEYWORDS
4-aminoantipyrine, metal complex, antifungal, antibacterial.

INTRODUCTION
Transition metal complexes derived from different heterocyclic ligands has relation with bio inorganic medicinal chemistry is widely explored (i-vi). The catalytic application of these complexes has been increasing interest in recent time (vii-x). Although transition metal complexes has been employed successfully as catalyst in different c-c cross coupling reaction by Negishi, Suzuki, Sonogashira (xi, xii). Schiff bases are consider as "Privileged ligands" due to complex formation ability with wide range of transition metal ions yielding stable and coloured metal complexes. Some complexes have been interesting physical, chemical and biological activity (xii, xiv). Schiff bases and their complexes of 4-aminoantipyrine and its derivative (xv) create great deal of interest in recent years. Metal- mediated antibiotic, antibacterial, antiviral, antipyretic radio sensitizing agent, and anticancer compounds, among which 4-aminoantipyrine and its complexes have been known to possess a variety of application in biological clinical, analytical and pharmacological areas; among which 4-aminoantipyrine and its complexes have been known to possess a variety of application in biological clinical, analytical, and pharmacological areas (xvi). The structure of the complexes is elucidated by using magnetic moment mass, elemental analysis, FTIR, 1H-NMR, 13C-NMR. The biological activity of the Schiff base and their metal complexes is reported.

EXPERIMENTAL AND MATERIALS

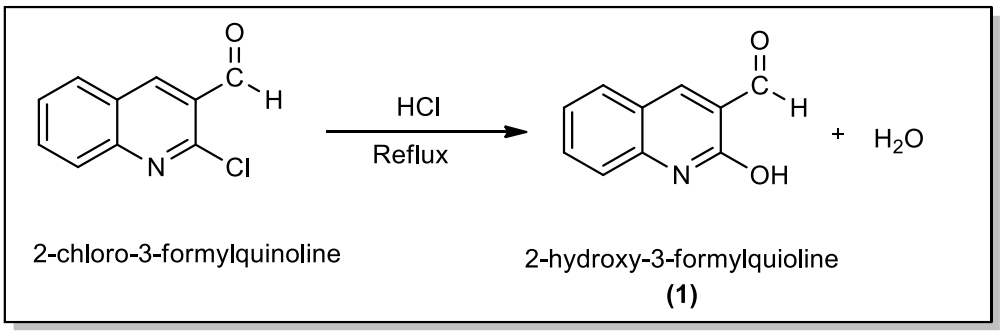
The material used for the synthesis of Schiff base ligand HFQAAPAHP (HL_A) are 4-aminoantipyrine, 2-chloro-3-formylquinoline, glacial acetic acid, 2-amino-3-hydroxypyridine. Analar sample of copper (II) chloride, nickel (II) chloride hexahydrated, cobalt (II) chloride hexahydrated and zinc chloride were used as such.

SYNTHESIS OF SCHIFF BASE: (HFQAAPAHP)

The 2-hydroxy-3-formylquinoline was selected for Schiff base. The various steps for the synthesis of 2-hydroxy-3-formylquinoline are given below.

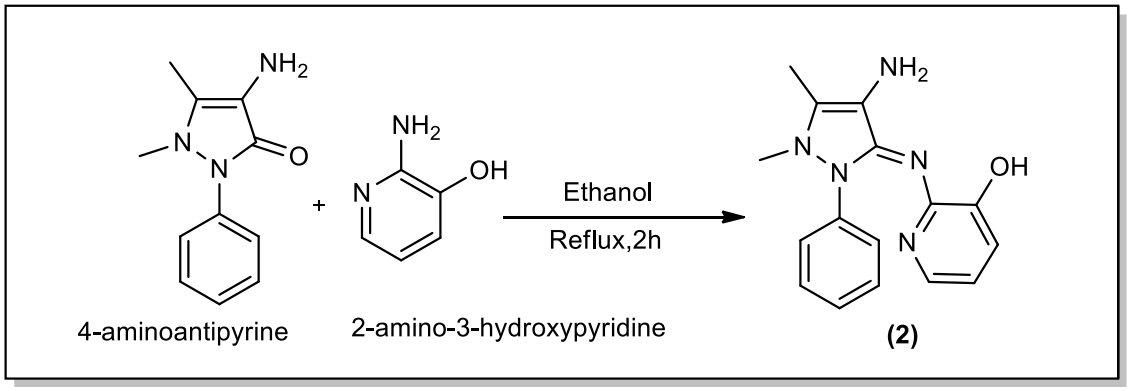
PROCEDURE FOR THE SYNTHESIS OF 2-HYDROXY-3-FORMYLQUINOLINE

2-chloro-3-formylquinoline (1) (0.1 M) was refluxed for 10 h in HCl (4M) and settled down at R.T. for cooling. The cooled reaction mixture was poured on crushed ice to get solid yellow product (xvii) and this product was recrystallized in acetic acid. (Yield 85%)

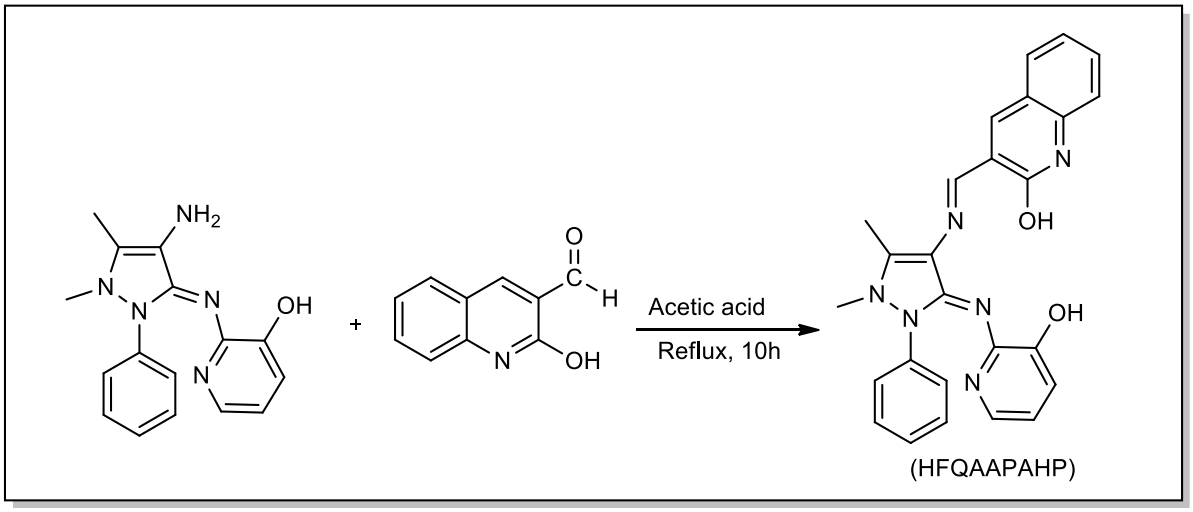


SYNTHESIS OF SCHIFF BASE FROM 4-AMINOANTIPYRINE AND 2-AMINO-3-HYDROXYPYRINE (HFQAAPAHP)

The synthesis of compound (2) was done by the method reported earlier (xviii). A hot solution of 4-aminoantipyrine (0.1 M) was mix with 2-amino-3-hydroxypyridine at hot condition in 30 ml of ethanol. The resulting mixture was precipitated after 2h of reflux. The solid was separated by filtration, purified by crystallisation from ethanol washed with diethyl ether and dried in vacuum over anhydrous calcium chloride. (Yield 88%)

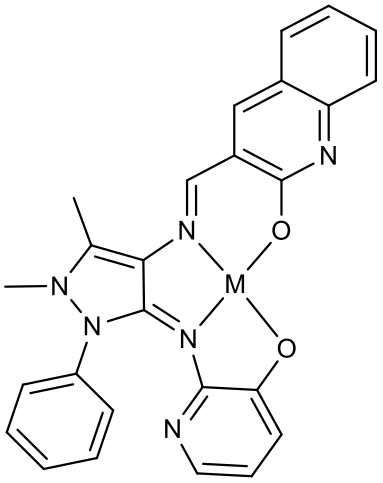


The Schiff base ligand was synthesised by equimolar amount of compound (1 & 2) were dissolved in hot ethanol solution, few drops of glacial acetic acid were added and the solution was refluxed for 10 h with continuous stirring, a solid Schiff base product formed was filtered and recrystallized from ethanol.(yield 75%)



SYNTHESIS OF METAL COMPLEXES

The Schiff base metal complexes were synthesized by a solution of ligands (HFQAAPAHP) (4 mM) in ethanol at hot condition was refluxed with an ethanolic solution of metal chloride (4mM) for about 3h. Then the solution was concentrated on water bath. The solid product formed was separated and washed thoroughly with hot ethanol.

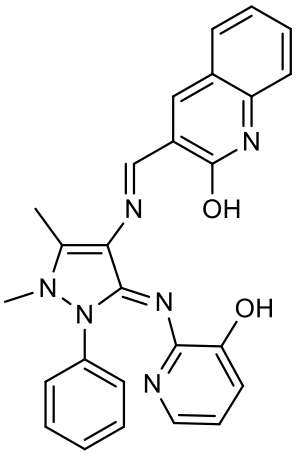
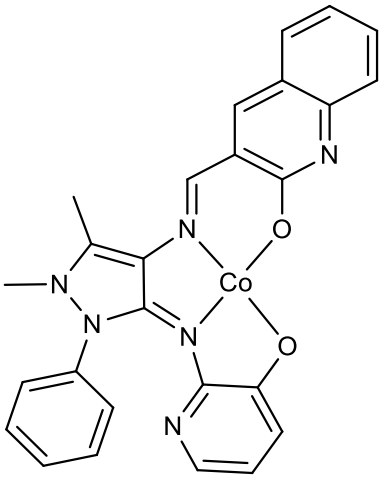
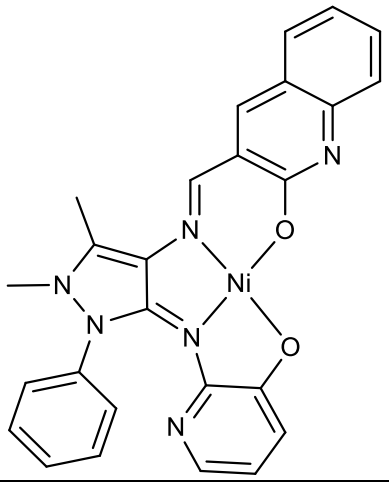


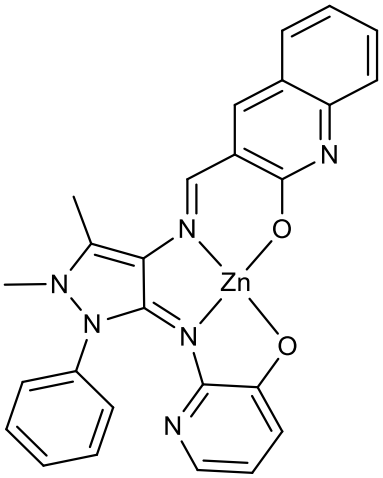
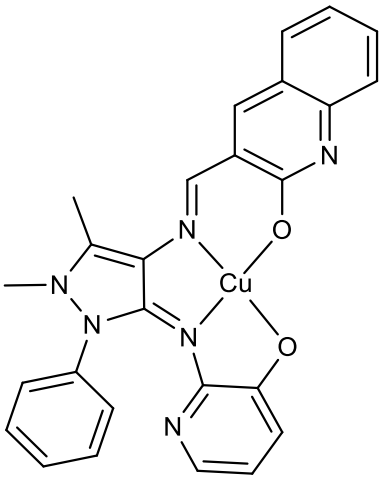
(HFQAAPAHP)

M= Co(II), Ni(II), Cu(II) and Zn(II)

Fig.1 Tentetive structure of metal complexes.

STUCTURE 0F METAL COMPLEXES

Entry	Product	Time	Yield (%)
L		10h	75
[CoL]		2-3 h	78
[NiL]		2-3h	80

[ZnL]		2-3h	74
[CuL]		2-3h	79

ELEMENTAL ANALYSIS

Compound	Empirical formula	Yield %	Colour	Calculated%				Formula weight	Mol. conductance(Λ)	Magnetic mom. $\mu_{eff.(B.M)}$
				M	C	H	N			
[H_2L]	$C_{26}H_{22}N_6O_2$	75	Orange red	-	71.71	4.86	16.08	450.5	-	-
[CoL]	$CoC_{26}H_{20}N_6O_2$	66	RED	11.92	63.16	4.28	14.17	507.4	7.4	3.72
[NiL]	$NiC_{26}H_{20}N_6O_2$	56	Brown	11.88	63.19	4.28	14.17	507.1	8.5	Dia
[CuL]	$CuC_{26}H_{20}N_6O_2$	58	Dark brown	12.73	62.58	4.24	14.04	512.0	9.8	1.73
[ZnL]	$ZnC_{26}H_{20}N_6O_2$	61	Light brown	13.05	62.35	4.23	13.98	511.8	7.8	Dia

I.R. SPECTRAL DATA OF SCHIFF BASE AND ITS COMPLEXES (cm^{-1})

Compound	υ (-OH group of 2-aminopyridine)	υ (OH-group of quinolone)	υ (C=N)	υ (M-N)	υ (M-O)
[H_2L]	3325	3058	1538,1630	-	-
[CoL]	-	-	1510,1616	433	525
[NiL]	-	-	1518,1612	429	566
[CuL]	-	-	1513,1582	493	588
[ZnL]	-	-	1532,1597	484	538

^{1}H-NMR AND ^{13}C-NMR SPECTRA

At room temperature, 1H-NMR spectra of Schiff base and zinc complex were recorded in $CDCl_3$. Multiple in the region 6.84δ – 7.54δ indicating Schiff base ligand (HFQAAPAHP) due to aromatic protons. The signal at 9.82δ attributable to the pyrazolone ring C-methyl and N-methyl group respectively. The hydroxyl group of 2-amino-3-hydroxypyridine and quinole moieties in the ligand are responsible for the peak at 10.83δ and 13.54δ. The lack of these peaks indicates zinc complex formation due to chelation of the –OH proton of quinolone and aminohydroxypyridine. The azomethine proton shift to downfield than Schiff base due to formation of metal complex. The deshielding of the azomethine proton due to formation of metal ligand coordination bond.

^{1}H-NMR SPECTRAL DATA OF SCHIFF BASE AND ITS ZINC COMPLEX (ppm)

compound	δ(H-aromatic)	δ(C-methyl)	δ(N-methyl)	δ(CH=N)	δ(OH of quinoline)	δ(OH of aminopyrine)
H_2L	6.84-7.54	2.41	3.17	9.83	13.54	10.83
ZnL	7.06	2.44	3.19	10.18	-	-

RESULT AND DISCUSSION

The Schiff base and its metal complexes have been analysed for their various antibacterial and pathogenic bacteria like Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, Staphylococcus aureus and fungal activity for Candida and fungal studies. The free ligand has observed less activity than its metal complexes. Lipophilic nature (xix, xx)of the metal complex has responsible for the greater activity than ligands. The faster diffusion of metal complexes as a whole through the cell membrane or combined activity of metal and ligand (xxi) result in to increase in the antibacterial activity. Overtone concept (xxii) and Tweedy chelation theory explain such increased activity of the metal complexes. The lipid membrane that surrounds the cell favours the passage of only lipid soluble materials according to Overton's concept of cell permeability which liposolubility is an important factor which decide the antibacterial activity.

ANTIMICROBIAL ACTIVITY DATA FOR THE SCHIFF BASE AND ITS COMPLEXS (PPM)

Compound	**E.coli**			**B.subtilis**			**S.aureus**		
	40	80	120	40	80	120	40	80	120
H2L	17	18	19	12	14	16	-	14	16
[CoL]	19	22	20	13	15	14	-	12	17
[NiL]	11	18	19	13	15	20	15	-	19
[CuL]	14	16	20	-	14	13	16	20	21
[ZnL]	11	16	21	14	12	15	16	19	-

CONCLUSSION

In this research article, we have presented the synthesis of Schiff base ligands and their later first-row transition metal (II) complexes. Various spectral data and elemental analysis confirmed the structure of Schiff base ligands and their metal complexes. Present research suggests the coordination of the ligand to the metal ion in N, N, O, O fashion. The prepared compound was found as non-electrolytic in nature**.** The prepared compound shows the moderate to excellent biological activity than its ligands

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